

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:

Xiaobin ZHAO

Appl. No. To be assigned (Cont. of  
PCT/GB00/00321)

Filed: August 2, 2001 (PCT File Date: 3  
February 2000)

For: **Process For The Production of  
Multiple Cross-Linked Hyaluronic  
Acid Derivatives**

Art Unit: To be assigned

Examiner: To be assigned

Atty. Docket: 0623.1110001/JMC/TMS

**Preliminary Amendment**

Commissioner for Patents  
Washington, D.C. 20231

Sir:

Before examining the above application, please amend the application as follows.

This Amendment is provided in the following format:

- (A) A clean version of each replacement paragraph/section/claim along with clear instructions for entry;
- (B) Starting on a separate page, appropriate remarks and arguments. 37 C.F.R. § 1.111 and MPEP 714; and
- (C) Starting on a separate page, a marked-up version entitled: "Version with markings to show changes made."

It is not believed that extensions of time or fees for net addition of claims are required beyond those that may otherwise be provided for in documents accompanying this paper. However, if additional extensions of time are necessary to prevent abandonment of this application, then such extensions of time are hereby petitioned under 37 C.F.R.

§ 1.136(a), and any fees required therefor (including fees for net addition of claims) are hereby authorized to be charged to our Deposit Account No. 19-0036.

***Amendments***

***In the Specification:***

On the first page of the specification, on the line following the title, please insert the following sentence -- This application is a continuation of International Application No. PCT/GB00/00321, filed on 3 February 2000, which was published under PCT Article 21(2) in English and which is fully incorporated herein by reference. --

***In the Claims:***

Please cancel claims 22 and 23.

Please substitute the following claim 3 for the pending claim 3:

3. (once amended) A process according to claim 1 wherein the crosslinking is effected by means of two or more different bonds selected from the group consisting of ether, ester, sulfone, amine, imino and amide bonds.

Please substitute the following claim 4 for the pending claim 4:

4. (once amended) A process according to claim 1 or claim 2 wherein the cross-linking agent is selected from the group consisting of formaldehyde, gluteraldehyde, divinyl sulfone, a polyanhydride, a polyaldehyde, a polyhydric alcohol, carbodiimide,

epichlorohydrin, ethylene glycol diglycidylether, butanediol diglycidylether, polyglycerol polyglycidylether, polyethylene glycol diglycidylether, polypropylene glycol diglycidylether, and a bis-or poly-epoxy cross-linker.

Please substitute the following claim 5 for the pending claim 5:

5. (once amended) A process according to claim 1 wherein an ether bond is formed using a crosslinking agent selected from the group consisting of bis epoxides and poly epoxides under alkaline conditions.

Please substitute the following claim 6 for the pending claim 6:

6. (once amended) A process according to claim 1 wherein an ester bond is formed using a crosslinking agent selected from the group consisting of bis epoxides and poly epoxides under acidic conditions.

Please substitute the following claim 7 for the pending claim 7:

7. (once amended) A process according to claim 5 wherein the crosslinker is selected from the group consisting of 1,2,3,4-diepoxymethane and 1,2,7,8-diepoxymethane.

Please substitute the following claim 8 for the pending claim 8:

8. (once amended) A process according to claim 1 wherein an ether bond is formed using a glutaraldehyde cross-linking agent under acidic conditions.

Please substitute the following claim 9 for the pending claim 9:

9. (once amended) A process according to claim 1 wherein the crosslinking of each type of functional group is effected sequentially.

Please substitute the following claim 11 for the pending claim 11:

11. (once amended) A process according to claim 9 wherein HA is first cross-linked via the hydroxyl groups by formation of ether bonds and subsequently cross-linked via the carboxyl groups by formation of ester bonds.

Please substitute the following claim 12 for the pending claim 12:

12. (once amended) A process according to claim 1 wherein the crosslinking of each type of functional group is effected simultaneously.

Please substitute the following claim 13 for the pending claim 13:

13. (once amended) A process according to claim 1 for preparing double crosslinked HA.

Please substitute the following claim 15 for the pending claim 15:

15. (once amended) Multiple cross-linked HA obtainable by a process according to claim 1.

Please substitute the following claim 17 for the pending claim 17:

17. (once amended) Cross-linked HA according to claim 15 wherein the crosslinking bonds are two or more selected from the group consisting of ether, ester, sulfone, amine, imino and amide bonds.

Please substitute the following claim 18 for the pending claim 18:

18. (once amended) Multiple cross-linked HA according to claim 15 in the form of a film.

Please substitute the following claim 19 for the pending claim 19:

19. (once amended) Multiple cross-linked HA according to claim 15 in the form of a gel.

Please substitute the following claim 20 for the pending claim 20:

20. (once amended) HA according to claim 15 which is double cross-linked HA.

Please substitute the following claim 21 for the pending claim 21:

21. (once amended) A product comprising multiple cross-linked HA according to claim 15.

***Remarks***

Applicants respectfully request that this Preliminary Amendment be entered by the Examiner. By the foregoing amendment, claims 3-9, 11-13, 15 and 17-21 are sought to be amended. Claims 22 and 23 are sought to be canceled. These changes are believed to introduce no new matter, and their entry is respectfully requested.


Upon entry of the foregoing amendment, claim 1-21 are pending in the application, with claims 1 and 16 being the independent claims.

Applicants respectfully request that this Preliminary Amendment under 37 C.F.R. § 1.111 be entered by the Examiner. If the Examiner believes that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this application is respectfully requested.

Respectfully submitted,

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for John M. Covert  
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**Version with markings to show changes made**

***In the claims:***

Please substitute the following claim 3 for the pending claim 3:

3. (once amended) A process according to claim 1 [or claim 2] wherein the crosslinking is effected by means of two or more different bonds selected from the group consisting of ether, ester, sulfone, amine, imino and amide bonds.

Please substitute the following claim 4 for the pending claim 4:

4. (once amended) A process according to [any of claims 1 to 3] claim 1 or claim 2 wherein the cross-linking agent is selected from the group consisting of formaldehyde, gluteraldehyde, divinyl sulfone, a polyanhydride, a polyaldehyde, a polyhydric alcohol, carbodiimide, epichlorohydrin, ethylene glycol diglycidylether, butanediol diglycidylether, polyglycerol polyglycidylether, polyethylene glycol diglycidylether, polypropylene glycol diglycidylether, [or] and a bis-or poly-epoxy cross-linker.

Please substitute the following claim 5 for the pending claim 5:

5. (once amended) A process according to [any of claims] claim 1 [to 4] wherein an ether bond is formed using a crosslinking agent selected from the group consisting of bis epoxides and poly epoxides under alkaline conditions.

Please substitute the following claim 6 for the pending claim 6:

6. (once amended) A process according to [any of claims] claim 1 [to 4] wherein an ester bond is formed using a crosslinking agent selected from the group consisting of bis epoxides and poly epoxides under acidic conditions.

Please substitute the following claim 7 for the pending claim 7:

7. (once amended) A process according to claim 5 [or claim 6] wherein the crosslinker is selected from the group consisting of 1,2,3,4-diepoxabutane and 1,2,7,8-diepoxooctane.

Please substitute the following claim 8 for the pending claim 8:

8. (once amended) A process according to [any of claims] claim 1 [to 4] wherein an ether bond is formed using a gluteraldehyde cross-linking agent under acidic conditions.

Please substitute the following claim 9 for the pending claim 9:

9. (once amended) A process according to [any of claims] claim 1 [to 8] wherein the crosslinking of each type of functional group is effected sequentially.

Please substitute the following claim 11 for the pending claim 11:

11. (once amended) A process according to claim 9 [or claim 10] wherein HA is first cross-linked via the hydroxyl groups by formation of ether bonds and subsequently cross-linked via the carboxyl groups by formation of ester bonds.

Please substitute the following claim 12 for the pending claim 12:



12. (once amended) A process according to [any of claims] claim 1 [to 8] wherein the crosslinking of each type of functional group is effected simultaneously.

Please substitute the following claim 13 for the pending claim 13:

13. (once amended) A process according to [any of claims] claim 1 [to 12] for preparing double crosslinked HA.

Please substitute the following claim 15 for the pending claim 15:

15. (once amended) Multiple cross-linked HA obtainable by a process according to [any of claims] claim 1 [to 14].

Please substitute the following claim 17 for the pending claim 17:

17. (once amended) Cross-linked HA according to claim 15 [or claim 16] wherein the crosslinking bonds are [selected from] two or more selected from the group consisting of ether, ester, sulfone, amine, imino and amide bonds.

Please substitute the following claim 18 for the pending claim 18:

18. (once amended) Multiple cross-linked HA according to [any of claims] claim 15 [to 17] in the form of a film.

Please substitute the following claim 19 for the pending claim 19:

19. (once amended) Multiple cross-linked HA according to [any of claims] claim 15 [to 17] in the form of a gel.

20. (once amended) HA according to [any of claims] claim 15 [to 19] which is double cross linked HA.

21. (once amended) A product comprising multiple cross-linked HA according to [any of claims] claim 15 [to 20].